the recitation of "40 kb" allegedly refer to "probe length and not its complexity." This assertion is believed to be in error. By reference to the specification, it can be seen that the recitation of 40 kb refers to probe complexity as claimed.

Throughout the specification, complexity of the probe rather than probe length is described. For example, at the very least at page 18, lines 10-14, the specification states:

> The invention provides methods and compositions for staining chromosomal material. The probe compositions of this invention at the current state of hybridization techniques are typically of high complexity, usually greater than about 50 kb of complexity, the complexity depending upon the application for which the probe is designed.

At page 19, lines 11-14, the specification states:

> This invention provides for nucleic acid probes that reliably stain targeted chromosomal materials in the vicinity of one or more suspected genetic rearrangements. Such nucleic acid probes useful for the detection of genetic rearrangements are typically of high complexity.

At page 20, lines 13-17, the specification states:

> Preferably, the chromosome specific reagents used to detect CML of this invention comprise nucleic acid sequences having a complexity of from about 50 kilobases (kb) to about 1 megabase (Mb), more preferably from about 50 kb to about 750 kb, and still more preferably from about 200 kb to about 400 kb.

The specification states at page 22, lines 9-16:

> The invention still further provides for high complexity nucleic acid probes which have been optimized for rapid, efficient and automated detection of genetic rearrangements.

One way to produce a probe of high complexity is to pool several or many clones, for example, phage, plasmid, cosmid, and/or YAC clones, among others, wherein each clone contains an insert that is capable of hybridizing to some part of the target in a genome. Another way to produce such a probe is to use the polymerase chain reaction (PCR).

More specifically with respect to "40 kb", at the very least at page 37, line 13 to page 38, line 13, the specification discusses complexity of the probe:

> The term "*complexity*" is defined herein according to the standard for nucleic acid complexity as established by Britten et al., Methods of Enzymol., 29:363 (1974). See also Cantor and Schimmel, Biophysical Chemistry: Part III: The Behavior of Biological Macromolecules, at 1228-1230 (Freeman and Co. 1980) for further explanation and exemplification of nucleic acid complexity.
>
> The *complexity* preferred for a probe composition of this invention is dependent upon the application for which it is designed. In general, the larger the target area, the more complex is the probe. It is anticipated that the *complexity* of a probe needed to produce a desired pattern of landmarks on a chromosome will decrease as hybridization sensitivity increases, as progress is made in hybridization technology. As the sensitivity increases, the reliability of the signal from smaller target sites will increase. Therefore, whereas from about a 40 kb to about a 100 kb target sequence may be presently necessary to provide a reliable, easily detectable signal, smaller target sequences should provide reliable signals in the future. Therefore, as hybridization sensitivity increases, a probe of a certain *complexity*, for example, 100 kb, should enable the user to detect considerably more loci in a genome than are presently reliably detected; thus, more information will be obtained with a probe of the same complexity. The term "*complexity*" therefore refers to the *complexity* of the total probe no matter how many visually distinct loci are to be detected, that is, regardless of the distribution of the target sites over the genome.
>
> As indicated above, with current hybridization techniques it is possible to obtain a reliable, easily detectable signal with a probe of about 40 kb to about 100 kb (eg. the probe insert capacity of one or a few cosmids) targeted to a compact point in the genome. Thus, for example, a *complexity*

> in the range of approximately 100 kb now permits hybridization to both sides of a tumor-specific translocation. (Italic emphasis supplied).
>
> The entire application thus describes probe complexity and not probe length.

It is clear from the application as a whole and the particular context of the recitation of "40 kb" that complexity of the probe, and not length as alleged by the Examiner, is being discussed. As shown *supra*, page 18-20 and 22 generally describe the invention as encompassing probes of "high complexity." At page 38, lines 8-13, immediately after discussing a probe of "about 40 kb to about 100 kb," the specification states "a complexity in the range of approximately 100 kb" (*see,* page 38, lines 8-13).

By review of the specification's description of the invention as encompassing probes of high complexity and the specific passages describing probes of "40 kb," it is clear that complexity is being referenced rather than probe length. No new matter is thus being added by these claims reciting a complexity of "40 kb."

The first page of the Official Action indicates that 3 sheets of PTO Form 1449 were attached. However, none of these sheets were attached to Applicants' copy. Applicants would appreciate if the Examiner could provide Applicants with a copy of the signed PTO Form 1449.

Further and favorable action in the form of a Notice of Allowance is respectfully requested.

In the event that there are any questions relating to this response, or to the application in general, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

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